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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,960	04/04/2001	Stephen L. Mayo	A-65353-7/RFT/RMS/RMK	7447

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EXAMINER
KIM, YOUNG J

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,960	MAYO ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 4/4/01.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-35 is/are rejected.

7)☒ Claim(s) 4-22 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has been assigned to Art Unit 1637. All further correspondence regarding this application should be directed to Group Art Unit 1637.

Claim Objections

Claims 4-22 are objected to because of the following informalities: claims 4-22 recite the limitation, "claim 1." However, claim 1 had been canceled by the preliminary amendment filed with the instant application (filed April 4, 2001), rendering the claims lacking in their proper antecedent basis. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 19-22 are product-by-process claims drawn to an optimized protein made by the method claims, a nucleic acid sequence encoding the optimized protein, an expression vector comprising the nucleic acid, and a host cell comprising the nucleic acid.

Claim 23 is drawn to any protein having a sequence that is at least about 5% different from any naturally occurring protein and at least 20% more stable.

MPEP states that:

"A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence" (MPEP 2163(a)).

The specification discloses a few protein sequences (Gβ1, FSD-1) and their optimization. However, the claims are drawn to any and every protein derived from the claimed process. The claims fail to disclose a correlation between the function and the structure of every protein, the nucleic acid encoding the protein, a vector comprising the nucleic acid, etc. Furthermore, there is no basis on which to search for what is being claimed. Because Applicants have not disclosed a sufficient number of species within the genus to which the claims are drawn, the claims lack in their written description as required under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-22 and 24-35 recite the limitation, "said protein." There is insufficient antecedent basis for this limitation in the claims. Amending the claims to recite, "said protein backbone structure," would overcome this rejection.

Claim 23 is indefinite for the recitation of the phrase, "known protein," because it becomes indefinite at which time frame and to whom the protein is considered to become known.

Claims 24-29 are indefinite because the claims do not have a conjunction (i.e., "and") after the first sub-step reciting the phrase, "protein backbone model," rendering the claims indefinite in their metes and bounds (i.e., what is included or excluded in/from the computer readable memory).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hardman (U.S. Patent No. 4,939,666, issued July 3, 1990).

Claim 23 is drawn to a protein sequence that is at least about 5% different from a known protein sequence that is at least 20% more stable than the known protein sequence.

Claims 24-28 are drawn to a computer readable memory that comprises a side chain module to correlate a group of potential rotamers (or residues) for residue positions of a protein backbone and ranking module that analyze the interaction of each of the rotamers with all or part of the remainder of the protein to generate a set of optimized protein sequences. Some

embodiments are drawn to the analyzer module comprising van der Waals, atomic solvation, hydrogen bonding, or secondary structure scoring functions.

Hardman discloses a computerized method/algorithm that determines/predicts a protein's three-dimensional structure (Abstract, column 2). Hardman discloses that the properties of protein depend directly from the protein's three-dimensional conformation and this conformation determines the activity or ability of enzymes, the capacity and specificity of binding proteins, and the structural attributes of receptor molecules, recognizing the need in the art for the means to stabilize a protein's three-dimensional structure (column 2, lines 1-9).

Hardman discloses the method process that each residue in consideration must be globally optimized (minimization of total energy, column 10, lines 32-33) as well (column 12, lines 1-12, column 15, lines 50-68) wherein each of the peptide block (or residue in question, or potential rotamer), must be examined for at least several target parameters. Such parameters are disclosed as hydrogen bonding (claim limitation 27, column 38), van der Waals (claim limitation 25, column 39), atomic solvation (or hydration contribution, claim limitation 24, column 39), and entropic contribution/angle-dependent strain, i.e., steric hindrance (or secondary structure of claim 26, column 39).

Hardman also contemplates the substitution of residues in the existing structure to further optimize the structure (column 19, lines 1-22).

Hardman conducts the disclosed method through an algorithm on a computer, necessarily requiring a computer readable memory as evidenced throughout the disclosure.

Finally, Hardman discloses the production of the polypeptide produced by this method which would necessarily allow the generation of the claimed polypeptide.

According to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to prove that prior art products do not necessarily or inherently posses characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; burden of proof is on applicant" (pp. 430). Absent evidence that the disclosed method of Hardman cannot produce the polypeptide of the claimed, the method of Hardman and the polypeptide produced from said method would inherently anticipate the claimed polypeptide.

Therefore, Hardman anticipates the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hardman (U.S. Patent No. 4,939,666, issued July 3, 1990) in view of Lee et al. (U.S. Patent No. 5,241,470, issued August 31, 1993).

Claims 24-28 are drawn to a computer readable memory that comprises a side chain module to correlate a group of potential rotamers (or residues) for residue positions of a protein backbone and ranking module that analyze the interaction of each of the rotamers with all or part of the remainder of the protein to generate a set of optimized protein sequences. Some

embodiments are drawn to the analyzer module comprising van der Waals, atomic solvation, hydrogen bonding, or secondary structure scoring functions.

Claim 29 is drawn to a computer readable memory further comprising an assessment module to assess the correspondence between the potential energy test results and theoretical potential energy data.

Hardman discloses a computerized method/algorithm that determines/predicts a protein's three-dimensional structure (Abstract, column 2). Hardman discloses that the properties of protein depend directly from the protein's three-dimensional conformation and this conformation determines the activity or ability of enzymes, the capacity and specificity of binding proteins, and the structural attributes of receptor molecules, recognizing the need in the art for the means to stabilize a protein's three-dimensional structure (column 2, lines 1-9).

Hardman discloses the method process that each residue in consideration must be globally optimized (minimization of total energy, column 10, lines 32-33) as well (column 12, lines 1-12, column 15, lines 50-68) wherein each of the peptide block (or residue in question, or potential rotamer), must be examined for at least several target parameters. Such parameters are disclosed as hydrogen bonding (claim limitation 27, column 38), van der Waals (claim limitation 25, column 39), atomic solvation (or hydration contribution, claim limitation 24, column 39), and entropic contribution/angle-dependent strain, i.e., steric hindrance (or secondary structure of claim 26, column 39).

Hardman also contemplates the substitution of residues in the existing structure to further optimize the structure (column 19, lines 1-22).

Hardman conducts the disclosed method through an algorithm on a computer, necessarily requiring a computer readable memory as evidenced throughout the disclosure.

Hardman does not disclose the comparison of the theoretical energy to the energy from the test data.

Lee et al. disclose a method of determining the packing conformation of amino acid side chains on a fixed peptide backbone wherein the side chains are "rotated" (thus rotamers) such that the side chains preferably settle in a low energy packing conformation (thus optimization) (Abstract, column 2, lines 1-25). Lee et al. also disclose that the conformation of energy of a peptide can be modified in many ways, ranging from potential energy functions having van der Waals, torsional biasing, electrostatic interactions, hydrogen bonding, hydrophobic interactions, entropic destabilization, cystein bond formation, etc. (column 10, lines 54-61).

Lee et al. disclose that in order to test the reliability and consistency of the method, seven predictions for one protein was made and each of these predictions were compared to that of the native structure (column 25, line 68 to column 26, line 24).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hardman and Lee et al. to arrive at the invention as claimed. One of ordinary skill in the art would have bee motivated to combine the teachings because by doing so, one of ordinary skill in the art would have been able to test the accuracy of the three-dimensional protein structure prediction as produced by Hardman. As the methods of Lee et al. and Hardman are directed in the art of protein structure prediction and optimization via computerized algorithm, one of ordinary skill in the art would have had a reasonable expectation

of success at combining the accuracy/reliability step of Lee et al. into the method of Hardman to arrive at the invention as claimed.

Therefore, the invention as claimed is obvious over the cited references.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 2-17 and 19-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2-27 and 38 of copending Application No. 09/837,886. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The claims are identical as illustrated below:

Instant Application	**U.S. Serial 09/837,886**
Claims 2-10	Claims 2-10 and 29-37
Claims 12-17	Claims 11-16 and 39-44
Claims 19-29	Claims 17-27 and 45-48*
Claim 11**	Claim 38

*Claims 45-48 of '886 application are identical to claims 19-22 of the instant application.

**Claim 11 is identical to claim 38 of the '886 application because claim 11 of the instant application has the same limitation as that of claim 38 of '886 application.

Claims 24-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 22-27 of copending Application No. 09/714,357. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The claims are identical in scope.

Claims 2-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2-29 and 31 of copending Application No. 09/812,034. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The claims are identical as illustrated below:

Instant Application	**U.S. Serial 09/812,034**
Claims 2-29	Claims 2-29
Claim 18	Claim 31*

*Claim 31 of the '034 application is identical to claim 18 of its own claim. Therefore, claim 18 of the instant application is identical to both, claims 18 and 31 of the '034 application.

Claim Rejections - 35 USC § 101 – Double Patenting

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain ***a*** patent therefor, subject to the conditions and requirements of this title.

Claims 6-10 and 12-17 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2-15 of prior U.S. Patent No. 6,188,965. This is a double patenting rejection.

Claims are identical (verbatim) as illustrated below:

Instant Application	U.S. Patent 6,188,965
Claim 2	Claim 6
Claims 3-5	Claims 3-5
Claim 7	Claim 6
Claims 8-10	Claims 7-9
Claims 12-17	Claims 10-15

Claim 18 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 2 of prior U.S. Patent No. 6,269,312. This is a double patenting rejection.

Claim 18 of the instant application is identical in scope to claim 2 of the '312 patent because all of the claimed limitation of claim 18 of the instant application (i.e., altering at least one supersecondary structure parameter value of a protein backbone structure) is included in claim 2 of the '312 patent.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 6, 11, and 19-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 6, 11, and 18-21 of U.S. Patent No.6,269,312. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reason.

Claims 6, 11, and 19-22 of the instant application are identical (verbatim) to claims 6, 11, and 18-21 of the '312 patent. Claims 6, 11, and 19-22 of the instant application depends from claim 6 or an independent claim 2. Likewise, claims 6, 11, and 18-21 of the '312 patent depend from claim 6 or an independent claim 2. The base claim 2 of the '312 patent differs from the base claim 2 in that it recites an additional sub-step of altering at least one supersecondary structure parameter value of a protein backbone structure. However, claim 2 of the instant application is open to additional intervening step since the method "comprises" the recited steps. Further, such modified step is considered to be a minor modification in the scope of the claims that is well within the purview of an ordinarily skilled artisan in the art of protein optimization, rendering the claims patentably indistinct.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of

such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

9/19/02

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
9/23/02